Early Journal Content on JSTOR, Free to Anyone in the World

This article is one of nearly 500,000 scholarly works digitized and made freely available to everyone in the world by JSTOR.

Known as the Early Journal Content, this set of works include research articles, news, letters, and other writings published in more than 200 of the oldest leading academic journals. The works date from the mid-seventeenth to the early twentieth centuries.

We encourage people to read and share the Early Journal Content openly and to tell others that this resource exists. People may post this content online or redistribute in any way for non-commercial purposes.

Read more about Early Journal Content at http://about.jstor.org/participate-jstor/individuals/early-journal-content.

JSTOR is a digital library of academic journals, books, and primary source objects. JSTOR helps people discover, use, and build upon a wide range of content through a powerful research and teaching platform, and preserves this content for future generations. JSTOR is part of ITHAKA, a not-for-profit organization that also includes Ithaka S+R and Portico. For more information about JSTOR, please contact support@jstor.org.

BACTERIOLOGY AND PATHOLOGY OF THE TONSILS WITH ESPECIAL REFERENCE TO CHRONIC ARTICULAR, RENAL, AND CARDIAC LESIONS.*

DAVID J. DAVIS.

(From the Laboratory of St. Luke's Hospital, Chicago.)

The relation of tonsillar infection to lesions existing in other regions, especially in the joints, heart, and kidneys, has received much attention, particularly from the clinical side. That a causal relationship not infrequently exists appears to be well recognized and is apparently based chiefly on the fact that often after tonsillectomy, in cases where there is reason to believe that such a causal relationship does exist, marked benefit or permanent cure follows. The bacteriological work that has been done in such cases is in many respects incomplete and unsatisfactory and in the study of cases of this nature, begun about three years ago, it appeared to be necessary in the first place to take up this phase of the problem with especial reference to organisms of the streptococcus and related groups.

Our knowledge of the bacteria of the tonsils has very largely been obtained from the study of swab cultures and smears made directly from the surface of the tonsils *in situ*. This surface is necessarily contaminated by bacteria from the mouth, throat, nose, food, inspired air, etc., and such examinations may not only give very incorrect data about the bacteria that actually exist in the depths of the tonsils but also may at least partly explain the reason why such a complex bacterial flora has been attributed to this organ.

Very early in this work, from a comparative study of the superficial and deeper flora in a number of cases, I became aware of the fact that swab surface cultures were of little value, because they revealed little or nothing about the bacteria in the crypts. Inasmuch as the latter are of far greater importance than the

---

* Received for publication January 15, 1912.

surface flora it became necessary to make careful cultures from the depths of the crypts as well as from the surface. The following technic in the examination of extirpated tonsils was therefore used: the excised tonsil was received in a clean receptacle or in clean gauze and, as soon as possible, smears and blood-agar plate cultures were made from the surface. The tonsil was then incised with a hot knife and from the crypts thus exposed similar smears and cultures were made. In many cases, for control, swab cultures of the surface were made before extirpation and compared with those made after.

The extirpated tonsils from 113 cases have been examined bacteriologically. Many more were examined grossly or microscopically, but for various reasons were not suitable for bacteriological work. The tonsils, usually more or less hypertrophied, were obtained from cases of joint lesions, nephritis, heart disease, tonsilitis, and some were examined also from cases of simple hypertrophy without serious complications. These conditions will be discussed separately.[1]

ARTHRITIS.

In this group are 28 cases, which include a variety of conditions ranging from simple articular pains associated with tonsilitis to severe chronic involvement. Some gave histories of having had typical attacks of acute articular rheumatism, but usually the arthritis was chronic in character with frequent more or less acute exacerbations. In some instances the arthritis was deforming and associated at times with exudates into the joints.

From the crypts hemolytic streptococci were obtained as the predominating organism in 25 cases. In many they were in pure growth and in large numbers. In two cases the pneumococcus predominated, though a few hemolytic streptococci were present also. In the remaining case the streptococcus mucosus was found, together with a few hemolytic streptococci. It will thus be seen that hemolytic streptococci were found in every case in the tonsils and predominated in nearly all.

---

[1] In discussing the bacteriology of these cases reference will be made chiefly to the predominating organisms on the plate culture. Manifestly occasional colonies of various organisms that have no importance whatever will appear on plates made under such conditions. These include moulds, chromogenic bacteria, white staphylococci, colon bacilli and the like. Such bacteria occurring sparsely and with no constancy on the plates were considered of no import and discarded. In anaerobic cultures made in a number of the cases the number and variety of bacteria obtained have been few and inconstant. It should be stated that in smears one not infrequently sees bacilli, often in considerable number, which so far have not been cultivated. More might be said about such organisms, but here it is sufficient to state that there is no reason to believe that they possess any pathologic significance. The term "pneumococcus" in this paper includes organisms which produce a green zone on blood-agar plates and which occur generally in diplococcus form. Many of these organisms grow in long chains; some ferment inulin, and others do not.

Rabbits were inoculated intravenously with streptococci from 17 of the joint cases. All but two strains caused lesions in the animals and in one instance, associated with the arthritis, was endocarditis of the tricuspid valve. Pneumococci from five cases, including the two in which they were predominant, were introduced into the veins of rabbits and in one animal non-fatal monoarticular arthritis developed.

Three of the cases of arthritis were complicated by chorea, either at the time of examination or sometime previously. They all revealed a predominant streptococcus flora in the tonsillar crypts, and upon injection of two of the strains into rabbits both developed acute multiple arthritis. Neither chorea nor endocarditis was noted in these animals.

In but two individuals suffering with severe chronic arthritis was it possible to obtain fluid from the joints. In both cases the fluid was straw-colored, slightly turbid, and some fibrin formed on standing. Polynuclear leukocytes were present but not in large numbers. The fluid and also the blood in these cases were sterile.

NEPHRITIS.

These cases, 10 in number, were chiefly chronic, and many had developed nephritis shortly after having had colds or tonsilitis. Some were mild, others very severe, and two were hemorrhagic in character. Two were complicated by arthritis. The tonsils as a rule were enlarged and the surfaces uneven and usually red. In nine of the 10 cases hemolytic streptococci were found predominating or pure in the tonsillar crypts. In some a few pneumococcus-like organisms appeared but were in no instance in large numbers. In the one case, which did not reveal streptococci, a small aerobic, gram-positive, non-liquefying, non-hemolytic bacillus was found nearly pure in the crypts. This bacillus did not produce gas in glucose, caused no change in milk, was non-motile, and 1 c.c. killed a guinea-pig in 24 hours. It was not identified.

Streptococci from eight of the 10 cases were injected intravenously into rabbits and in all localization in joints or tendon sheaths occurred. The kidneys in these animals were examined with negative results. In the urine from a number of these animals there was no evidence of abnormal constituents and no streptococci were found.

ENDOCARDITIS.

There were 10 cases of endocarditis, nearly all of which were, at the time, suffering from arthritis or gave a history of having had it in the past. They were as a rule not severe, excepting two, which were malignant in character.

Hemolytic streptococci were found in six cases in large numbers and predominatingly. In the remaining cases were large numbers of pneumococci and in two these organisms were nearly pure. In one case of fatal malignant endocarditis with pneumococci in the blood and in the pleural and pericardial exudates the tonsils were only slightly enlarged, but near the base they were very fibrous, and in the depths contained small pockets filled with pus cells and diplococci. In the cultures from the crypts pneumococci grew almost pure, there being only an occasional streptococcus colony. Streptococci from four cases were injected into rabbits and arthritis developed in all. The pneumococci from three of the cases of endocarditis were injected into rabbits and vegetative endocarditis developed in two instances; no joint lesions.

TONSILLAR HYPERTROPHY.

The tonsils were examined from 61 cases of tonsillar hypertrophy, nearly all of whom gave histories of repeated attacks of tonsilitis. In 50 the hemolytic streptococcus was obtained as the predominant organism and, as in the other groups, in many instances the cultures were practically pure. In only two were pneumocci predominant, and in these some streptococci were also found. In one case the streptococcus mucosus was found in considerable numbers and in six cases the white staphylococcus was the most numerous organism. In three cases the influenza bacillus was found predominant and on the blood-agar plates they appeared in enormous numbers in symbiosis with the few hemolytic streptococci also present. These are the only three instances in the entire series in which the influenza bacillus was found in the tonsillar crypts. Two of these three strains were tested on guinea-pigs and intraperitoneal injections of two blood-agar slant growths killed the animals in 24 hours; one slant-agar growth was not sufficient, as a rule, to cause death. In two cases typical diphtheria bacilli were found nearly pure in the crypts. In one case of recurrent tonsilitis, the last attack being four weeks previous to the tonsillectomy, cultures from the crypts gave a nearly pure growth of this organism, while cultures from the surface both before and after extirpation did not reveal it. This bacillus was fatal to a guinea-pig by intraperitoneal inoculation. There is some reason to believe that this case was responsible for an outbreak of diphtheria in a number of persons closely associated with this individual. In the second case, while the bacilli were typical morphologically, they were not pathogenic for guinea-pigs and therefore should be classed in the pseudodiphtheria group. In one case from this group a nearly pure growth of *B. mucosus capsulatus* was found in the crypts. Not infrequently an isolated colony of this bacillus appeared on the plate cultures but not in predominating or significant numbers.

Seven strains of streptococci from the cases of recurring tonsilitis were tested on rabbits and in every instance the animal developed arthritis in every way similar to that produced by streptococci from the other clinical groups. Four strains of pneumococci from these cases including the strains which predominated in two cases were injected into rabbits with negative results. In one remarkable case of multiple neuritis without arthritis or heart lesions, in the crypts of the hypertrophied tonsils was a nearly pure growth of hemolytic streptococci which produced a fatal multiple arthritis in rabbits.

The arthritis which develops in the animals injected with streptococci is manifested by the occurrence of lameness and swelling of the joints and usually appears from the third to the fifth day after inoculation. If too large doses are given the animal may die of septicemia in 24 or 48 hours, but even this early the joints may be involved, as shown by redness of the lining membranes and the presence in the cavity of a few leukocytes and streptococci. The most suitable dose is the 24-hour growth from the surface of one small blood-agar slant. On the whole the strains isolated from the various cases are quite uniform in their pathogenic properties, a given dose in animals of uniform size usually producing similar results. Of far greater importance is the size and age of the animal. Large full-grown or old animals are resistant and indeed may withstand enormous doses (several slant-agar growths); on the other hand, young animals are so susceptible that even very small doses may give rise to septicemia and death in 24 hours or less without definite localization of the infection. Half to three-quarter grown animals are most suitable for this work.

Some of the animals die in the course of one to three weeks, but in many the joint lesions gradually subside and the animal recovers. In the less severe cases few joints or only one may be isolated, but usually the arthritis is multiple and in some of the rabbits almost every joint in the body was attacked, including the vertebral joints. The carpal joints and the joints of the hind limbs are often the seat of localization. In a number of animals the process became chronic, the joints increasing in size with marked destruction of bone and joint surfaces. In one case subluxation occurred after six weeks. Chronic joint abscesses may arise in which streptococci in few numbers may be found in the glary mucoid or mucopurulent contents, and such animals often live for months, gradually becoming very emaciated and badly crippled, but nevertheless appearing quite lively and eating normally. Ultimately most of them die, but usually without a septicemia. Streptococci may be found in few numbers in the chronic lesions, though in some instances the cultures were negative. In four animals, following non-fatal injections, the joints simulated a deforming arthritis. They became large and exostoses appeared about the ends of the bone. After several months the deformities in these cases gradually and apparently entirely disappeared.

The pathogenicity of a number of the streptococci was tested further by injecting them intraperitoneally into guinea-pigs. It was found that one culture almost invariably sufficed to kill by peritonitis in 24–48 hours.

A monkey (*macacus rhesus*) was given an intracardiac injection of a strain of streptococcus which had produced arthritis in a rabbit and been reisolated from one of the joints of the animal. After a few days multiple arthritis involving many joints on both fore and hind limbs appeared and death followed in about two weeks. The joints contained an abundant purulent exudate from which streptococci were cultivated. The heart's blood also contained them in moderate numbers, but there was no sign of endocarditis and no localization in any other part of the body.

Post-mortem examination of the animals revealed the fact that not infrequently in the early stages the involvement was periarticular and often extended to the tendon sheaths. At times, especially in the hind limbs, a tendon sheath might be involved throughout its entire length and the joint cavities remain entirely free.

Microscopic examination of sections through the extremities have been made in some of the animals. This work is being carried on at present in a systematic way in order to examine the joints at definite intervals following the inoculation, but the results are not yet complete. It would appear from the data at hand that the organisms first localize in the subserous structures about the joints, forming small infected foci, and from here secondarily break into the cavities.

The exudate in the joints early is glary and mucoid and soon becomes purulent, containing large numbers of polynuclear cells and streptococci. Usually abundant phagocytosis of this organism in the exudate is noted. After a week or longer, in some rabbits but not in all, the exudate may become thick and pasty. Streptococci can ordinarily be readily grown from these joint exudates, but a few exceptions have been noted. In one animal that died on the fifth day with definite arthritis, the cocci could be seen in the leukocytes, but careful cultures on blood media gave no growth. In two other instances though the involvement of the joint was unmistakable no organisms grew in the cultures.

In the bodies of the inoculated animals careful search was made for other lesions, especially endocarditis. Following streptococcus injections in only one instance was a lesion found, vegetative in character on the tricuspid valve. This was not extensive but was definite, and was produced by a strain isolated originally from the tonsillar crypts in a case of multiple arthritis. The joints of the animal were also involved but there was no other localization. The organisms were recovered from the heart's blood. Pericarditis was not found in any instance.

As stated above, in two instances pneumococci produced an endocarditis. In one case, by intracardiac injection, a very extensive mitral endocarditis developed in an animal, associated with large renal infarcts and septicemia but without joint lesions. This organism, which fermented inulin and gave the typical green zone on blood agar, was isolated from the depth of a tonsil in a case of severe multiple arthritis, not associated at the time, so far as could be determined clinically, with heart lesions. In this case also streptococci were abundant in the tonsils and upon intravenous inoculation into an animal produced arthritis. In the second case a definite but less extensive mitral endocarditis was produced by intravenous injection with pneumococci from the depths of the tonsils in a case of recurrent tonsilitis associated with endocarditis. From the valvular lesions the organism was recovered pure. It did not, even in huge doses, produce arthritis in animals.

Some of the strains of pneumococci were injected into animals in enormous doses without effect. This was true even in those instances where endocarditis did develop and is in marked contrast with the fact that streptococci produce arthritis in very much smaller doses. In only one instance with a pneumococcus-like organism did a joint lesion develop and this was not fatal.

Observations were made with the view of determining possible differences in the various strains of streptococci isolated from the clinical groups. On blood-agar plates these streptococci are alike, in that they are all hemolytic. The width of the zone of hemolysis may vary considerably. I have noted at times even on the same plate two kinds of hemolytic streptococci. The one possesses a wide distinct zone of hemolysis with a rather large gray central colony, and is the ordinary typical streptococcus pyogenes; the other, met with only occasionally, has a much narrower zone, which may be slightly turbid, and the margin is less distinct and the central colony smaller. The difference is sufficient to enable one to separate them clearly, especially when they occur on the same plate. The latter organism forms as a rule shorter chains but shows no tendency to occur in pairs in the chain. It grows less luxuriantly in subcultures, and tends to die out more quickly. It produces typical arthritis on injection into rabbits but less readily than the more hemolytic variety, and on sugars they cannot be differentiated. It does not ferment inulin. It is surely not a pneumococcus, never producing a green zone on blood plates and not possessing the lanceolate form. After passage through an animal it still retains its properties. I am inclined to consider it a less virulent form of the ordinary hemolytic streptococcus.

Forty-three strains from the crypts of the tonsils from the various clinical groups were tested on dextrose, lactose, mannite, raffinose, and inulin, the acidity being determined after five days by titration with NaOH. Without going into minute details it will be sufficient to state that all produced acid in dextrose and none in raffinose and inulin. All but five fermented lactose, one of these strains coming from a case of arthritis, the other four from cases of enlarged tonsils with recurring tonsilitis. Eleven strains fermented mannite and 32 did not. The five strains which failed to ferment lactose failed to ferment mannite also. The grouping into mannite and non-mannite fermenters has no evident relation whatever to the clinical condition. For instance, some streptococci isolated from the arthritis cases fermented mannite and others did not. This applies also to the other clinical groups. Compared with streptococci from other sources (puerperal fever, erysipelas, empyema, scarlet fever), they show no morphologic or cultural differences. Five strains of pneumococci were tested on sugars. Two fermented inulin and three did not. The latter three include the two strains that produced endocarditis in the animals. Otherwise they behaved alike, fermenting dextrose and lactose but not mannite or raffinose. They rapidly acidify and coagulate milk, especially if the milk is mixed with equal parts of broth.

THE MICROSCOPIC EXAMINATION OF THE TONSILS.

The tonsils generally were moderately hypertrophied with often red and smooth or coarsely lobulated surfaces. In some instances they were very large, the crypts deep and tortuous, and at times contained yellowish caseous masses. Many, especially those from persons giving a history of repeated tonsilitis for a long time, were very fibrous, particularly at the base, and the crypts were much distorted.

Microscopically the most striking feature was the common occurrence of polynuclear leukocyte clusters far down at the end of the branching crypts. In some instances these appeared as if they were in the tonsillar tissue beneath the epithelium, but this was not true. The epithelium, especially in the hypertrophied tonsils, often along the course of the crypts becomes very thin and permeated with lymphoid cells. The two layers of epithelium come in close apposition and as a thin layer penetrate far into the depths of the tonsils. Often at the farthest extremity of such structures or possibly along the course or in a small lateral crypt one may find small clusters of polymorphonuclear cells, among which by proper staining methods bacteria, especially streptococci, may be found. The difficulty of proper drainage of such foci can well be appreciated.

Not uncommonly one finds, deep in the tonsil cavities containing bacteria, cholesterin crystals, hyalin material, and cellular débris and lined by epithelium. Occasionally similar structures are seen in which the lining epithelium has entirely disappeared and the connective tissue cells may be observed penetrating the mass while about the cholesterin crystals large multinucleated giant cells appear. Such cavities have undoubtedly been formed by adhesions or constrictions at the outlet of the crypts preventing drainage, and should pathogenic bacteria be present in such foci it can readily be understood how an abscess might form. I have observed in the series four small abscesses deep in the tonsils near the capsule, which were filled with thick pus and surrounded by a dense fibrous wall; the contents of three of these were sterile, no organisms being found either in smears or culture. In the adjacent crypts, however, in each case were myriads of streptococci. The abscesses were undoubtedly present for a long time and the organisms which initiated the infection later in all probability died. In the one case in which the purulent contents was not sterile a mixture of streptococci and staphylococci were found.

There appears to be little or no difference in the lesions of the tonsils obtained from the various clinical groups. For example the recurrent tonsilitis cases may present changes identical with those seen in the articular, cardiac, or renal cases. In general the more numerous the attacks of tonsillar trouble have been the more extensive is the fibrosis and the more distorted are the crypts.

In all tonsils from individuals who are more than a few weeks old plasma cells are found in abundance. They occur under the epithelium, especially that lining the crypts, along the connective tissue bundles and about the blood vessels. In the hypertrophied tonsils they are much more numerous. Their significance is not entirely understood, but inasmuch as they are more or less characteristic of chronic inflammatory processes they probably indicate a chronic infection of the tonsillar crypts or the absorption of toxic substances therefrom.

In four of the 10 cases of endocarditis it was noted that pneumococcus-like organisms were found in large numbers or nearly pure in the tonsillar crypts, while they rarely occurred, as we have seen, in other conditions. This fact is interesting because these pneumococci are apparently identical with the common so-called endocarditic cocci. In one of the malignant endocarditis cases, as above stated, this organism was obtained in the tonsillar crypts nearly pure and in the heart's blood, pleural and pericardial fluids. The data at hand are not sufficient to permit definite assertions, but it appears that these organisms which are normally found on the buccal mucosa and which have been called *Str. viridans* (Schottmüller), *Str. salivarius* (Gordon), and are known by many other names, are not often found in the crypts. I am inclined to believe that under certain conditions they may invade the crypts, especially if the tonsils have been previously diseased, as in cases of acute articular rheumatism, and it is possible that their virulence may be thus increased and that they may enter the circulation from the diseased tonsil and localize on the valves of the heart. It is known that such cocci obtained from normal mouths may produce experimental endocarditis in rabbits.[1]

In this connection may be mentioned the work of Rosenow[2] on endocarditis. He has isolated by blood culture in a series of cases an organism which he believed to be a modified pneumococcus, and by intravenous and intracardiac injection of large and repeated doses into animals he was able to produce endocarditis with many of these strains. This organism appears to be the same as the organism isolated from the tonsils of heart cases described above, and like them too it very rarely produces arthritis in animals. He is of the opinion that in two of his cases the infection probably came from the tonsils, though apparently tonsillar cultures were not made.

It is not intended in this paper to discuss in detail the therapeutic effect of removal of the tonsils. It is sufficient to state that the improvement in many cases in the various clinical groups following tonsillectomy has been marked, resulting often in complete cure. In some the trouble was arrested while in a few no effect was noted. Favorable results have been obtained by many others, as is commonly known. Perhaps the therapeutic results furnish the best argument we have so far in favor of the idea that the infected tonsils bear some relationship to arthritic, renal, cardiac, and other clinical conditions. The evidence in this respect seems amply sufficient in many cases to localize definitely the source of trouble in the tonsils. Furthermore, the occurrence in the tonsils, as was found repeatedly in our series, of a pure or nearly pure growth of hemolytic streptococci with no evidence whatever, so far as our present technical methods indicate, of any other significant germ, would seem to point to this organism as the etiological organism in these cases.

The mere fact that these various strains of streptococci from tonsils are capable of causing joint lesions in animals is perhaps in itself not of great significance. It has been shown by others, particularly by Cole, Harris, and Beattie, that streptococci from various sources will produce arthritis in animals. I have produced arthritis in rabbits with typical hemolytic streptococci isolated from normal tonsils of individuals who never had had anything more than the usual colds common to nearly everyone. It is of interest that the various strains from cardiac, renal, arthritic, and other cases, and even the strains from normal tonsils, are apparently identical not only in their cultural reactions, especially in sugars, but also in their pathogenic properties in animals. I think it should be pointed out that while streptococci may be the causative organisms in many of these cases, they do not appear to be specific for the various clinical conditions. The reason why in one case nephritis is produced and in another, for instance, an arthritis, probably lies in the varying local susceptibility of the tissues of the individual rather than in any peculiar specificity of the infecting organisms.

---

[1] *Jour. Path. and Bact.*, 1911, 15, p. 323.

[2] *Jour. Infect. Dis.*, 1909, 6, p. 245.

SUMMARY.

In a series of cases including chronic articular, renal, and cardiac affections, and chronic tonsilitis, the crypts of the extirpated tonsils generally revealed the hemolytic streptococcus as the predominating organism and in some cases in practically pure growth.

A few exceptions were noted, especially in endocarditis, in which a pneumococcus-like organism was predominant.

The hemolytic streptococci are virulent for rabbits and other animals, invariably localizing in or about the joints and producing multiple arthritis. It only occasionally localizes on the heart valves. The pneumococci rarely produce arthritis but frequently localize on the heart valves.

The multiple arthritis in animals may become chronic, lasting for months. The exudate is mucoid early, later becoming purulent; usually it contains streptococci though in a few instances it was sterile.

The streptococci isolated from the various clinical groups of cases are alike in their morphology, their reactions in media including sugars, and also in their pathogenicity for animals.

The bacterial flora of the surface of the tonsils as revealed by a study of these chronic cases is usually strikingly different from the flora of the crypts. They may occasionally be similar but usually

they are not. Subcultures as ordinarily made from the surface of the tonsils, especially in chronic infections, are quite unreliable for determining the crypt flora.

The crypts of enlarged tonsils in nearly all cases contain large numbers of virulent streptococci and these cases may therefore be considered as streptococcus carriers.

A large part of this work was done at the Memorial Institute for Infectious Diseases, Chicago, and most of the material was obtained from the service of Dr. Frank Billings at the Presbyterian Hospital. Material was also received from Dr. J. L. Miller, Dr. Joseph Capps, Dr. George Shambaugh, Dr. Dyas, Dr. G. W. Post, and several other physicians, to all of whom I wish here to acknowledge my indebtedness and express my thanks.